MARKED UP COPY OF AMENDED CLAIMS
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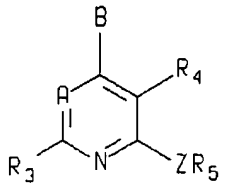
1.(TWICE AMENDED) A compound of the formula



I

or a pharmaceutically acceptable salt thereof, wherein

A is $-CR_7$;

B is $-NR_1R_2$, $-CR_1R_2R_{11}$, $-C(=CR_2R_{12})R_1$, $-NHCHR_1R_2$, $-OCHR_1R_2$, $-SCHR_1R_2$, $-CHR_2OR_1$, $-CHR_1OR_2$, $-CHR_2SR_1$, $-C(S)R_2$, $-C(O)R_2$, $-CHR_2NR_1R_2$, $-CHR_1NHR_2$, $-CHR_1N(CH_3)R_2$, or $-NR_{12}NR_1R_2$;

Z is NH, O, S, $-N(C_1-C_2$ alkyl), $-NC(O)CF_3$, or $-C(R_{13}R_{14})$, wherein R_{13} and R_{14} are each, independently, hydrogen, trifluoromethyl or methyl, or one of R_{13} and R_{14} is cyano and the other is hydrogen or methyl, or $-C(R_{13}R_{14})$ is a cyclopropyl group, or Z is nitrogen or CH and forms a five or six membered heterocyclic ring fused with R_5, which ring optionally includes two or three further hetero members selected independently from oxygen, nitrogen, NR_{12}, and $S(O)_m$, and optionally includes from one to three double bonds, and is optionally substituted with halo, C_1-C_4 alkyl, $-O(C_1-C_4$ alkyl), NH_2, $NHCH_3$, $N(CH_3)_2$, CF_3, or OCF_3, with the proviso that said ring does not include any –S-S-, -S-O-, -N-S-, or –O-O- bonds, and does not include more than two oxygen or $S(O)_m$ heterologous members;

R_1 is C(O)H, $C(O)(C_1-C_6$ alkyl), $C(O)(C_1-C_6$ alkylene)$(C_3-C_8$ cycloalkyl), $C(O)(C_3-C_8$ cycloalkylene)$(C_3-C_8$ cycloalkyl), $C(O)(C_1-C_6$ alkylene)$(C_4-C_8$ heterocycloalkyl), $-C(O)(C_3-C_8$ cycloalkylene)$(C_4-C_8$ heterocycloalkyl), C_1-C_6 alkyl, C_3-C_8 cycloalkyl, C_4-C_8 heterocycloalkyl, $-(C_1-C_6$ alkylene)$(C_3-C_8$ cycloalkyl), $-(C_3-C_8$ cycloalkylene)$(C_3-C_8$ cycloalkyl), $-(C_1-C_6$ alkylene)$(C_4-C_8$ heterocycloalkyl), $-(C_3-C_8$ cycloalkylene)$(C_4-C_8$ heterocycloalkyl), or –O-aryl, or $-O-(C_1-C_6$ alkylene)-aryl; wherein said aryl, C_4-C_8 heterocycloalkyl, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, C_3-C_8 cycloalkylene, and C_1-C_6 alkylene groups may each independently be optionally substituted with from one to six fluoro and may each independently be optionally substituted with one or two substituents R_8 independently selected from the group consisting of C_1-C_4 alkyl, $-C_3-C_8$ cycloalkyl, hydroxy, chloro, bromo, iodo, CF_3, $-O-(C_1-C_6$ alkyl), $-O-(C_3-C_5$ cycloalkyl), $-O-CO-(C_1-C_4$ alkyl), $-O-CO-NH(C_1-C_4$ alkyl), $-O-CO-N(R_{24})(R_{25})$, $-N(R_{24})(R_{25})$, $-S(C_1-C_4$ alkyl), $-S(C_3-C_5$ cycloalkyl), $-N(C_1-C_4$alkyl)$CO(C_1-C_4$ alkyl), $-NHCO(C_1-C_4$ alkyl), $-COO(C_1-C_4$ alkyl), $-CONH(C_1-C_4$ alkyl), $-CON(C_1-C_4$ alkyl)$(C_1-C_2$ alkyl), CN, NO_2, $-OSO_2(C_1-C_4$ alkyl), $S^+(C_1-C_6$ alkyl)$(C_1-C_2$ alkyl)I^-, $-SO(C_1-C_4$ alkyl) and $-SO_2(C_1-C_4$

alkyl); and wherein the C_1-C_6 alkyl, C_1-C_6 alkylene, C_5-C_8 cycloalkyl, C_5-C_8 cycloalkylene, and C_5-C_8 heterocycloalkyl moieties of R_1 may optionally independently include from one to three double or triple bonds; and wherein the C_1-C_4 alkyl moieties and C_1-C_6 alkyl moieties of R_8 can optionally independently be substituted with hydroxy, amino, C_1-C_4 alkyl, aryl, -CH_2-aryl, C_3-C_5 cycloalkyl, or –O-(C_1-C_4 alkyl), and can optionally independently be substituted with from one to six fluoro, and can optionally include one or two double or triple bonds; and wherein each heterocycloalkyl group of R_1 includes from one to three heteromoieties selected from oxygen, $S(O)_m$, nitrogen, and NR_{12};

R_2 is hydrogen, C_1-C_{12} alkyl, C_3-C_8 cycloalkyl, C_4-C_8 heterocycloalkyl, -(C_1-C_6 alkylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), -(C_1-C_6 alkylene)(C_4-C_8 heterocycloalkyl), -(C_3-C_8 cycloalkylene)(C_4-C_8 heterocycloalkyl), aryl, –(C_1-C_6 alkylene)aryl, or -(C_3-C_8 cycloalkylene)(aryl); wherein each of the foregoing R_2 groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, and C_1-C_6 alkyl, wherein one of said one to three substituents can further be selected from bromo, iodo, C_1-C_6 alkoxy, -OH, -O-CO-(C_1-C_6 alkyl), -O-CO-N(C_1-C_4 alkyl)(C_1-C_2 alkyl), -S(C_1-C_6 alkyl), -S(O)(C_1-*C_6 alkyl), -$S(O)_2$(C_1-C_6 alkyl), S^+(C_1-C_6 alkyl)(C_1-C_2 alkyl)I^-, CN, and NO_2; and wherein the C_1-C_{12} alkyl, -(C_1-C_6 alkylene), -(C_5-C_8 cycloalkyl), -(C_5-C_8 cycloalkylene), and -(C_5-C_8 heterocycloalkyl) moieties of R_2 may optionally independently include from one to three double or triple bonds; and wherein each heterocycloalkyl group of R_2 includes from one to three heteromoieties selected from oxygen, $S(O)_m$, nitrogen, and NR_{12};

or when R_1 and R_2 are as in –$NHCHR_1R_2$, -$OCHR_1R_2$, -$SCHR_1R_2$, –CHR_1R_2 or -NR_1R_2, R_1 and R_2 of B may form a saturated 5- to 8-membered ring which may optionally include one or two double bonds and in which one or two of the ring carbons may optionally be replaced by an oxygen, $S(O)_m$, nitrogen or NR_{12}; and which ring can optionally be substituted with from 1 to 3 substituents selected from the group consisting of hydroxy, C_1-C_4 alkyl, fluoro, chloro, bromo, iodo, CF_3, -O-(C_1-C_4 alkyl), -O-CO-(C_1-C_4 alkyl), -O-CO-NH(C_1-C_4 alkyl), -O-CO-N(C_1-C_4 alkyl)(C_1-C_2 alkyl), -NH(C_1-C_4 alkyl), -N(C_1-C_2 alkyl)(C_1-C_4 alkyl), -S(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)CO(C_1-C_4 alkyl), -NHCO(C_1-C_4 alkyl),-COO(C_1-C_4 alkyl), -CONH(C_1-C_4 alkyl), -CON(C_1-C_4 alkyl)(C_1-C_2 alkyl), CN, NO_2, -OSO_2(C_1-C_4 alkyl), -SO(C_1-C_4 alkyl), and –SO_2(C_1-C_4 alkyl), wherein one of said one to three substituents can further be selected from phenyl;

R_3 is methyl, ethyl, fluoro, chloro, bromo, iodo, cyano, methoxy, OCF_3, NH_2, NH(C_1-C_2 alkyl), $N(CH_3)_2$, -$NHCOCF_3$, -$NHCH_2CF_3$, $S(O)_m$(C_1-C_4 alkyl), $CONH_2$, -$CONHCH_3$, $CON(CH_3)_2$, -CF_3, or CH_2OCH_3;

R_4 is hydrogen, C_1-C_4 alkyl, C_3-C_5 cycloalkyl, -(C_1-C_4 alkylene)(C_3-C_5 cycloalkyl), -(C_3-C_5 cycloalkylene)(C_3-C_5 cycloalkyl), cyano, fluoro, chloro, bromo, iodo, -OR_{24}, C_1-C_6 alkoxy, -O-(C_3-C_5 cycloalkyl), -O-(C_1-C_4 alkylene)(C_3-C_5 cycloalkyl), -O-(C_3-C_5 cycloalkylene)(C_3-C_5 cycloalkyl), -$CH_2SC(S)O(C_1$-C_4 alkyl), -CH_2OCF_3, CF_3, amino, nitro, -$NR_{24}R_{25}$, -(C_1-C_4 alkylene)-OR_{24}, -(C_1-C_4 alkylene)Cl, -(C_1-C_4 alkylene)$NR_{24}R_{25}$, -$NHCOR_{24}$, -$NHCONR_{24}R_{25}$, -C=NOR_{24}, -$NHNR_{24}R_{25}$, -

$S(O)_mR_{24}$, $-C(O)R_{24}$, $-OC(O)R_{24}$, $-C(O)CN$, $-C(O)NR_{24}R_{25}$, $-C(O)NHNR_{24}R_{25}$, and $-COOR_{24}$, wherein the alkyl and alkylene groups of R_4 may optionally independently include one or two double or triple bonds and may optionally independently be substituted with one or two substituents R_{10} independently selected from hydroxy, amino, $-NHCOCH_3$, $-NHCOCH_2Cl$, $-NH(C_1\text{-}C_2$ alkyl), $-N(C_1\text{-}C_2$ alkyl)$(C_1\text{-}C_2$ alkyl), $-COO(C_1\text{-}C_4$ alkyl), $-COOH$, $-CO(C_1\text{-}C_4$ alkyl), $C_1\text{-}C_6$ alkoxy, $C_1\text{-}C_3$ thioalkyl, cyano and nitro, and with one to four substituents independently selected from fluoro and chloro;

R_5 is aryl or heteroaryl and is substituted with from one to four substituents R_{27} independently selected from halo, $C_1\text{-}C_{10}$ alkyl, $-(C_1\text{-}C_4$ alkylene)$(C_3\text{-}C_8$ cycloalkyl), $-(C_1\text{-}C_4$ alkylene)$(C_4\text{-}C_8$ heterocycloalkyl), $-(C_3\text{-}C_8$ cycloalkyl), $-(C_4\text{-}C_8$ heterocycloalkyl), $-(C_3\text{-}C_8$ cycloalkylene)$(C_3\text{-}C_8$ cycloalkyl), $-(C_3\text{-}C_8$ cycloalkylene)$(C_4\text{-}C_8$ heterocycloalkyl), $C_1\text{-}C_4$ haloalkyl, $C_1\text{-}C_4$ haloalkoxy, nitro, cyano, $-NR_{24}R_{25}$, $-NR_{24}COR_{25}$, $-NR_{24}CO_2R_{26}$, $-COR_{24}$, $-OR_{25}$, $-CONR_{24}R_{25}$, $-CO(NOR_{22})R_{23}$, $-CO_2R_{26}$, $-C{=}N(OR_{22})R_{23}$, and $-S(O)_mR_{23}$; wherein said $C_1\text{-}C_{10}$ alkyl, $C_3\text{-}C_8$ cycloalkyl, $(C_1\text{-}C_4$ alkylene), $(C_3\text{-}C_8$ cycloalkyl), $(C_3\text{-}C_8$ cycloalkylene), and $(C_4\text{-}C_8$ heterocycloalkyl) groups can be optionally substituted with from one to three substituents independently selected form $C_1\text{-}C_4$ alkyl, $C_3\text{-}C_8$ cycloalkyl, $(C_1\text{-}C_4$ alkylene)$(C_3\text{-}C_8$ cycloalkyl), $-(C_3\text{-}C_8$ cycloalkylene)$(C_3\text{-}C_8$ cycloalkyl), $C_1\text{-}C_4$ haloalkyl, hydroxy, $C_1\text{-}C_6$ alkoxy, nitro halo, cyano, $-NR_{24}R_{25}$, $-NR_{24}COR_{25}$, $NR_{24}CO_2R_{26}$, $-COR_{24}$, $-OR_{25}$, $-CONR_{24}R_{25}$, CO_2R_{26}, $-CO(NOR_{22})R_{25}$, and $-S(O)_mR_{23}$; and wherein two adjacent substituents of the R_5 group can optionally form a 5-7 membered ring, saturated or unsaturated, fused to R^5, which ring optionally can include one, two, or three heterologous members independently selected from O, $S(O)_m$, and N, but not any –S-S-, -O-O-, -S-O-, or –N-S- bonds, and which ring is optionally substituted with $C_1\text{-}C_4$ alkyl, $C_3\text{-}C_8$ cycloalkyl, $-(C_1\text{-}C_4$ alkylene)$(C_3\text{-}C_8$ cycloalkyl), $-(C_3\text{-}C_8$ cyloalkylene)$(C_3\text{-}C_8$ cycloalkyl), $C_1\text{-}C_4$ haloalkyl, nitro, halo, cyano $-NR_{24}R_{25}$, $NR_{24}COR_{25}$, $NR_{24}CO_2R_{26}$, $-COR_{24}$, $-OR_{25}$, $-CONR_{24}R_{25}$, CO_2R_{26}, $-CO(NOR_{26})R_{25}$, or $-S(O)_mR_{23}$; wherein one of said one to four optional substituents R_{27} can further be selected from $-SO_2NH(C_1\text{-}C_4$ alkyl), $-SO_2NH(C_1\text{-}C_4$ alkylene)$(C_3\text{-}C_8$ cycloalkyl), $-SO_2NH(C_3\text{-}C_8$ cycloalkyl), $-SO_2NH(C_3\text{-}C_8$ cycloalkylene)$(C_3\text{-}C_8$ cycloalkyl), $-SO_2N(C_1\text{-}C_4$ alkyl)$(C_1\text{-}C_2$ alkyl), $-SO_2NH_2$, $-NHSO_2(C_1\text{-}C_4$ alkyl), $-NHSO_2(C_3\text{-}C_8$ cycloalkyl), $-NHSO_2(C_1\text{-}C_4$ alkylene)$(C_3\text{-}C_8$ cycloalkyl), and $-NHSO_2(C_3\text{-}C_8$ cycloalkylene)$(C_3\text{-}C_8$ cycloalkyl); and wherein the alkyl, and alkylene groups of R_5 may independently optionally include one double or triple bond;

R_6 is hydrogen, $C_1\text{-}C_6$ alkyl, $C_3\text{-}C_8$ cycloalkyl, $-(C_1\text{-}C_6$ alkylene)$(C_3\text{-}C_8$ cycloalkyl), or $-(C_3\text{-}C_8$ cycloalkylene)$(C_3\text{-}C_8$ cycloalkyl), wherein said alkyl and cycloalkyl may optionally be substituted with one hydroxy, methoxy, ethoxy or fluoro group;

R_7 is hydrogen, methyl, fluoro, chloro, bromo, iodo, cyano, hydroxy, $-O(C_1\text{-}C_2$ alkyl), -O(cyclopropyl), $-COO(C_1\text{-}C_2$ alkyl), $-COO(C_3\text{-}C_8$ cycloalkyl), $-OCF_3$, CF_3, $-CH_2OH$, or CH_2OCH_3;

R_{11} is hydrogen, hydroxy, fluoro, ethoxy, or methoxy;

R_{12} is hydrogen or $C_1\text{-}C_4$ alkyl;

R_{22} is independently at each occurrence selected from hydrogen, $C_1\text{-}C_4$ alkyl, $C_1\text{-}C_4$

haloalkyl, C_3-C_6 alkenyl, C_3-C_6 alkynyl, C_3-C_8 cycloalkyl, (C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), and (C_1-C_4 alkylene)(C_3-C_8 cycloalkyl);

R_{23} is independently at each occurrence selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_2-C_8 alkoxyalkyl, C_3-C_8 cycloalkyl, -(C_1-C_4 alkylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), aryl, -(C_1-C_4 alkylene)aryl, piperidine, pyrrolidine, piperazine, N-methylpiperazine, morpholine, and thiomorpholine;

R_{24} and R_{25} are independently at each occurrence selected from hydrogen, -C_1-C_4 alkyl, C_1-C_4 haloalkyl, especially CF_3, -CHF_2, CF_2CF_3, or CH_2CF_3, -(C_1-C_4 alkylene)OH, -(C_1-C_4 alkylene)-O-(C_1-C_4 alkyl), -(C_1-C_4 alkylene)-O-(C_3-C_5 cycloalkyl), C_3-C_8 cycloalkyl, -(C_1-C_4 alkylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), -C_4-C_8 heterocycloalkyl, -(C_1-C_4 alkylene)(C_4-C_8 heterocycloalkyl), -(C_3-C_8 cycloalkylene)(C_4-C_8 heterocycloalkyl), aryl, and -(C_1-C_4 alkylene)(aryl), wherein the -C_4-C_8 heterocycloalkyl groups can each independently optionally be substituted with aryl, CH_2-aryl, or C_1-C_4 alkyl, and can optionally include one or two double or triple bonds; or, when R_{24} and R_{25} are as $NR_{24}R_{25}$, -$C(O)NR_{24}R_{25}$, -(C_1-C_4 alkylene)$NR_{24}R_{25}$, or -$NHCONR_{24}R_{25}$, then $NR_{24}R_{25}$ may further optionally form a 4 to 8 membered heterocyclic ring optionally including one or two further hetero members independently selected from $S(O)_m$, oxygen, nitrogen, and NR_{12}, and optionally including from one to three double bonds;

R_{26} is independently at each occurrence selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_3-C_8 cycloalkyl, -(C_1-C_4 alkylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), aryl, and -(C_1-C_4 alkylene)(aryl); and

wherein each m is independently zero, one, or two,

with the proviso that heterocycloalkyl groups of the compound of formula I[~~, II, or III~~] do not include any –S-S-, -S-O-, -N-S-, or –O-O- bonds, and do not include more than two oxygen or $S(O)_m$ heterologous members.

9. (AMENDED) A pharmaceutical composition for the treatment of (a) a disorder or condition the treatment of which can be effected or facilitated by antagonizing CRF, or (b) a disorder or condition selected from inflammatory disorders such as rheumatoid arthritis and osteoarthritis, pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic; phobias, including social phobia, agoraphobia, and specific phobias; obsessive-compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception such as fibromyalgia; mood disorders such as depression, including major depression, single episode depression, recurrent depression, child abuse induced depression, mood disorders associated with premenstrual syndrome, and postpartum depression; dysthemia; bipolar disorders; cyclothymia; chronic fatigue syndrome; stress-induced headache; [~~cancer;~~] irritable bowel syndrome[~~, Crohn's disease~~]; spastic colon; post operative ileus; ulcer; diarrhea; stress-induced fever; [~~human immunodeficiency virus infections;~~] neurodegenerative diseases such as

Alzheimer's disease, Parkinson's disease and Huntington's disease; gastrointestinal diseases; [~~eating disorders such as anorexia and bulimia nervosa;~~] hemorrhagic stress; chemical dependencies or addictions, including dependencies or addictions to alcohol, cocaine, heroin, benzodiazapines, or other drugs; drug or alcohol withdrawal symptoms; stress-induced psychotic episodes; euthyroid sick syndrome; syndrome of inappropriate antidiuretic hormone; [~~obesity; infertility;~~] head trauma; spinal cord trauma; ischemic neuronal damage, including cerebral ischemia, for example cerebral hippocampal ischemia; excitotoxic neuronal damage; epilepsy; stroke; immune dysfunctions including stress induced immune dysfunctions, including porcine stress syndrome, bovine shipping fever, equine paroxysmal fibrillation, confinement dysfunction in chicken, sheering stress in sheep, and human-animal interaction stress in dogs; muscular spasms; urinary incontinence; senile dementia of the Alzheimer's type; multiinfarct dementia; amyotrophic lateral sclerosis; hypertension; tachycardia; congestive heart failure; osteoporosis[~~;~~] and premature birth[~~; hypoglycemia, and Syndrome X~~] in a mammal or bird, comprising an amount of a compound according to claim 1 that is effective in the treatment of such disorder or condition, and a pharmaceutically acceptable carrier.

10. (AMENDED) A method for the treatment of (a) a disorder or condition the treatment of which can be effected or facilitated by antagonizing CRF, or (b) a disorder or condition selected from inflammatory disorders such as rheumatoid arthritis and osteoarthritis, pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic; phobias, including social phobia, agoraphobia, and specific phobias; obsessive-compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception such as fibromyalgia; mood disorders such as depression, including major depression, single episode depression, recurrent depression, child abuse induced depression, mood disorders associated with premenstrual syndrome, and postpartum depression; dysthemia; bipolar disorders; cyclothymia; chronic fatigue syndrome; stress-induced headache; [~~cancer;~~] irritable bowel syndrome[~~, Crohn's disease~~]; spastic colon; post operative ileus; ulcer; diarrhea; stress-induced fever; [~~human immunodeficiency virus infections;~~] neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and Huntington's disease; gastrointestinal diseases; [~~eating disorders such as anorexia and bulimia nervosa;~~] hemorrhagic stress; chemical dependencies or addictions, including dependencies or addictions to alcohol, cocaine, heroin, benzodiazapines, or other drugs; drug or alcohol withdrawal symptoms; stress-induced psychotic episodes; euthyroid sick syndrome; syndrome of inappropriate antidiuretic hormone; [~~obesity; infertility;~~] head trauma; spinal cord trauma; ischemic neuronal damage, including cerebral ischemia, for example cerebral hippocampal ischemia; excitotoxic neuronal damage; epilepsy; stroke; immune dysfunctions including stress induced immune dysfunctions, including porcine stress syndrome, bovine shipping fever, equine paroxysmal fibrillation, confinement dysfunction in chicken, sheering stress in sheep, and human-animal interaction stress in dogs; muscular spasms; urinary incontinence;

senile dementia of the Alzheimer's type; multiinfarct dementia; amyotrophic lateral sclerosis; hypertension; tachycardia; congestive heart failure; osteoporosis~~[;]~~ and premature birth~~[; hypoglycemia, and Syndrome X]~~ in a mammal or bird, comprising administering to a subject in need of said treatment an amount of a compound according to claim 1, that is effective in treating such disorder or condition.

17. A pharmaceutical composition for treating a condition comprising a compound of claim 1 in an amount effective to treat said condition and a pharmaceutically acceptable carrier, wherein said condition is selected from the group consisting of:

a) abnormal circadian rhythm;

b) depression, further wherein a second compound for treating depression is administered, said second compound for treating depression having an onset of action that is delayed with respect to that of said ~~[CRF antagonist]~~ compound of claim 1; and

c) emesis.